Pulmonary sequestration and aspergillosis

Pascal Berna, El Djoulene Lebied, Jalal Assouad, Christophe Foucault, Claire Danel, Marc Riquet*

Service de Chirurgie Thoracique, Hôpital Européen Georges Pompidou, 20 rue Leblanc, 75015 Paris, France

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Abstract

Objective: Pulmonary sequestration (PS) is an uncommon congenital disease. Symptoms when present are usually secondary to pyogenic infection. Our objective was to draw attention on superimposed fungal infection. Methods: During the last 20 years, we operated upon 19 intralobar PS. Four of six patients operated during the last decade proved to have intralobar PS containing *Aspergillus*. Results: In one patient aspergillosis presented as an aspergilloma and communications between the sequestration and small bronchi were present. In another patient diagnosis was made before operation because of positive precipitins test. In two patients aspergillosis was discovered by the pathologist. Conclusions: Review of literature demonstrates PS fungal colonization to be a rare but recently reported entity (14 cases reported). The observation of four consecutive patients leads us to suggest that PS aspergillosis must be considered in order to evaluate its incidence.

Keywords: Pulmonary sequestration; Aspergillosis; Surgery

1. Introduction

Pulmonary sequestration (PS) is an uncommon congenital disease. Symptoms, when present are usually secondary to superimposed infections which are usually pyogenic in nature [1]. Other superimposed infections are extremely rare: Savic et al. [1] reported six cases associated with tuberculous and one nocardia infection in 540 published PS cases. Superimposed fungal infection has been reported only rarely consisting in isolated case reports. Aspergillosis appears the most frequent superimposed fungal infectious agent and requires more considerations.

2. Patients and methods

During the last 20 years we operated on 19 intralobar PS: 13 during the first decade (1985–1994) and six during the second (1995–2004). Among the 6 second decade patients, 4 (66%) proved to have superimposed fungal infection. All these patients were HIV negative. This report relates our experience with this particular location of aspergillosis.

3. Results

3.1. Patient 1

A 43-year-old homeless man was admitted because of a seizure following abundant alcohol intake. He was a heavy smoker and drinker and presented with left lower lobe pneumonia. After 3 months of antibiotics therapy, chest X-ray demonstrated a left lower lobe residual cavitary lesion. Bronchoscopy was negative for cancer. Bacteriologic cultures were negative for tuberculosis. Results of blood tests were normal. Computed Tomography (CT) scan demonstrated the lesion to be cystic and heterogeneous, suggesting possibility of PS. He underwent surgery following rehabilitation. Vascular and bronchial structure presented no particularity except for presence of an anomalous systemic artery arising from the aorta supplying the cystic mass, which confirmed the diagnosis of PS. A left lower lobe segmentectomy was performed. Pathology confirmed an intralobar polycystic sequestration and Grocott Staining demonstrated *Aspergillus hyphae* within the cystic lesions. The postoperative course was uneventful and the patient was discharged on the seventh postoperative day. He was faring well 8 years later.

3.2. Patient 2

A 46-year-old man, heavy smoker, presented with aggravating exertional dyspnea. Past medical history was
uneventful except for repeated rhinitis; chest X-ray demonstrated a left retrocardiac shadow.

Results of blood tests were normal. Dyspnea was related to an obstructive bronchopathy and was improved by bronchodilators. Bronchoscopy was normal. CT scan demonstrated a tissular, irregular mass which was suggestive of lung cancer. The patient underwent surgery. The left lower lobe mass was supplied by an anomalous artery arising from the aorta without presenting other vascular nor bronchial abnormality. A left lower lobectomy was performed. Pathology confirmed the diagnosis of intralobar PS. Grocott staining demonstrated *Aspergillus hyphae* within cystic lesions. The postoperative course was uneventful and the patient was discharged on the 12th postoperative day. He was faring well 9 years later.

### 3.3. Patient 3

A 54-year-old female was admitted with a chief complaint of cough associated with sputum and fever. She reported repeated episodes of pneumonia over the last 5 years and had been treated by antibiotics. Blood stained sputum was present for over one year. Past medical history was significant for allergic rhinitis since adolescence. Physical examination was normal. Results of blood tests were normal. Sputum and blood cultures were negative. Chest radiography revealed an opacity in the right lower lobe. On CT scan there was a cystic lesion of the posterior basal segment of the right lower lobe (Fig. 1).

Bronchoscopic examination was normal. An aortoangiogram showed this cystic lesion deriving its arterial blood supply from a collateral of the coeliac artery passing through the pulmonary ligament. The diagnosis of PS was made and a right lobectomy performed. Pathology demonstrated colonisation of the cystic cavities by aspergilloma and described communications between some cavities and the bronchi (Fig. 2). The patient post operative course was uneventful. The patient was discharged on post operative day 8 and was faring well 26 months later.

### 3.4. Patient 4

A 23-year-old female was admitted for minor and recurrent hemoptysis without fever occurring for a few weeks. Her past medical history was insignificant and physical examination was unremarkable. The chest X-ray showed an excavated opacity of the right lower lobe. The CT scan demonstrated cystic areas in the apical segment of the right lower lobe taking contrast. Blood tests demonstrated positive precipitins results for *Aspergillus*. Bronchoscopy was normal and a right lower lobectomy was performed. During surgery an abnormal artery originating from below the diaphragm was found when dissecting the pulmonary ligament. There was no other vascular nor bronchial abnormality. Pathology confirmed the diagnosis of aspergilloma (*Aspergillus niger*) within intralobar pulmonary sequestration, but failed to demonstrate communications between cavities and bronchi. The post operative course was uneventful and the patient was discharged on post operative day 5. The patients was readmitted 7 days following surgery with a pneumothorax due to a bronchial fistula which was treated by chest tube drainage, and was faring well 20 months later.

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*Fig. 1. Patient 3 CT scan (two images); right lower lobe sequestration presenting cystic lesions demonstrating aspergilloma.*
4. Comment

PS are rare anomalies in which a local area of a lung is supplied separately by an anomalous artery arising from the abdominal aorta or one of its branches. When the PS is right sided, the anomalous artery most frequently arises from the abdominal aorta (Table 1) as also observed in both our right sided cases. In intralobar sequestration (ILS), the isolated portion is anatomically part of a normal lobe within the same visceral pleura as in our patients. In extralobar sequestration (ELS), the isolated tissue is separated from the normal lung, and covered by its own visceral pleura [2]. The size and extent of the sequestered area are variable. The anomalous tissue is usually truly sequestered but in about 20% of cases, there is communication with normal bronchi [2]. Symptoms, when present, are usually secondary to superimposed infections which are usually pyogenic [1]; Superimposed infection of PS by fungal pathogens are extremely rare. Some are exceptional as those due to Blastomycosis dermatitidis [3] or to Exophiala [4]. Superimposed infection by Aspergillus was reported as of 1964 [5]; To our knowledge only 14 other cases have been reported (Table 1) [6–19]; all were case reports. All cases but one were observed in adults [7] and 2/3 occurred in females. Cough and sputum were the most frequent symptoms. Hemothysis present in two of our patients was reported in only one other observation [8]. When asymptomatic, cases were following the appearance of an abnormal shadow on chest X-rays. In two patients abnormal shadows were associated with increased tumor serum markers (CA19-9 [14,16]; CEA and CA 125 [16]): PS aspergillosis was diagnosed after surgery. In both these cases serum tumor markers returned to normal following surgery without further explanation and in both cases production of tumor markers was demonstrated in bronchial epithelium of the sequestered lung. PS aspergillosis is in fact essentially discovered after surgery. However, it may be suspected by preoperative positive precipitins as in our fourth patient [7,9,12,15,17], by positive sputum [17] or by CT guided biopsy [11,15,19]. In one case [7] diagnosis was provided only by precipitin positivity. In two patients it was obtained by PS culture [13,14]; In all other patients Aspergilloma or Aspergillus hyphae were identified within the resected specimens as in three of our patients. Aspergillus fumigatus was present in most cases; Aspergillus niger observed in our first patient has been reported only once [17].

PS were intralobar except in one patient [14]. Aspergillosis develop when the fungus colonises and proliferates in preexisting cavities [12]; The airways are thought to be the source of infection. The occurrence of a fungal mycetoma within an ILS indicates that the ILS must have some communications with the tracheobronchial tree [10,12], as

Table 1
PS and aspergillosis (review)

<table>
<thead>
<tr>
<th>First author</th>
<th>Year published</th>
<th>Age, sex</th>
<th>Site of disease</th>
<th>Blood supply</th>
<th>Clinical events</th>
<th>Aspergillus diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reboul [5]</td>
<td>1964</td>
<td>38, F</td>
<td>LLL, ILS</td>
<td>nf</td>
<td>Cough, sputum, mass</td>
<td>Aspergilloma</td>
</tr>
<tr>
<td>Mattila [6]</td>
<td>1965</td>
<td>37, M</td>
<td>LLL, ILS</td>
<td>na</td>
<td>Tuberculosis</td>
<td>Aspergilloma</td>
</tr>
<tr>
<td>Hwang [8]</td>
<td>1985</td>
<td>28, M</td>
<td>RLL, ILS</td>
<td>Aorta D</td>
<td>Hemothysis, cough</td>
<td>Aspergilloma</td>
</tr>
<tr>
<td>Uppal [10]</td>
<td>1993</td>
<td>36, F</td>
<td>LLL, ILS</td>
<td>IPA</td>
<td>Cough, pain</td>
<td>Aspergilloma</td>
</tr>
<tr>
<td>Kugai [14]</td>
<td>1996</td>
<td>34, M</td>
<td>LLL, EL</td>
<td>nf</td>
<td>Mass CA 19.9</td>
<td>Postoperative culture</td>
</tr>
<tr>
<td>Sekiya [16]</td>
<td>1999</td>
<td>44, F</td>
<td>LLL, ILS</td>
<td>nf</td>
<td>Mass, CA 19.9, CA 125 CEA</td>
<td>Aspergillus hyphae</td>
</tr>
<tr>
<td>Niimis [18]</td>
<td>2003</td>
<td>45, F</td>
<td>LLL, ILS</td>
<td>Aorta D</td>
<td>Cough, sputum</td>
<td>Aspergiloma</td>
</tr>
</tbody>
</table>

RLL, right lower lobe; LLL, left lower lobe; F, Female; M, Male; nf, not found; na, not available; ILS, intralobar sequestration; ELS, extralobar sequestration; IPA, inferior phrenic artery; Aorta A, abdominal aorta; Aorta D, descending aorta.

Fig. 2. Communication between sequestered lung tissue and bronchus—(HES, ×100). Bronchus and bronchial epithelium (arrow); sequestration area (arrow head); Aspergilloma (*).
present in 20% cases [2], and as we could observe in one patient (n=3). For some authors [10,12], presence of Aspergillus supports the hypothesis that some ILS may be acquired lesions related to chronic infection rather than congenital abnormalities related to the abnormal development of lung buds, in which case connection with the airway would be absent. PS aspergillosis was observed in only one patient with ELS [14]. In this case, ELS presented as an abnormal shadow on chest X-ray associated with elevated CA 19-9. Aspergillus infection was demonstrated in the sequestered lung by postoperative culture.

The risk of developing aspergillosis in intralobar PS is not yet established. Therefore, it is not possible to define a group of patients that may represent a higher risk population for fungal infection. The first case was reported 40 years ago [5] but two-thirds of case reports were published during the last 10 years. This raises the question of an increased incidence of this colonisation but this could also be due to a more systematic research of Aspergillus fumigatus in Pathology practice. Two of our patients presented also with rhinitis, the one was allergic (patient 4) which was an independent disease and the other (patient 3) was infectious and may have contributed to PS contamination, but sinus aspergillosis was not documented. In the literature one patient was reported to have associated allergic rhinitis [8] but no patient had sinus aspergillosis.

In conclusion, observation of four patients and review of the literature lead us to suggest that PS aspergillosis is either misdiagnosed or becoming more frequent, and that Aspergillus must be looked for at work up for PS. Whatever the type of PS, preoperative diagnosis of aspergillosis should be an additional argument for surgery in all cases of sequestration even when asymptomatic.

References